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THE INFLUENCE OF CHAULMOOGRA OIL ON THE TUBERCLE BACILLUS

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Chaulmoogra oil has been advocated as a remedy for leprosy for many years, and interest in the subject has been greatly renewed by the investigations of Heiser,¹ who has reported a series of cases either apparently cured or greatly improved by intramuscular injections of mixtures of chaulmoogra oil, camphorated oil and resorcin. Subsequent reports by Hopkins,² McCoy and Hollmann,³ Coghill,⁴ Hall,⁵ Cadbury⁶ and Hollmann and Dean,⁷ have indicated that these chaulmoogra mixtures have a definite curative effect in leprosy.

As the *B. leprae* is an acid-fast micro-organism, these results naturally suggest that chaulmoogra oil may be destructive for other acid-fast bacilli, notably the tubercle bacillus, and at the suggestion of Dr. Jay F. Schamberg our experiments were undertaken with a virulent strain of bovine tubercle bacilli. While the work was under way, the excellent paper of Walker and Sweeny⁸ was published. These investigators have found that the sodium salts of the total fatty acids of chaulmoogra oil (chaulmoogrates) possess an extremely high bactericidal and antiseptic activity for the tubercle bacillus in vitro. By incorporating these salts in fluid culture mediums, they have found that dilutions as high as 1:100,000 are bactericidal and 1:1,000,000 may be antiseptic. Furthermore, these chaulmoogrates were found highly specific for acid-fast bacilli, similar experiments with other micro-organisms including *B. coli* and staphylococci, showing an absence of antiseptic activity in dilutions as low as 1:1,000. The authors also give a complete review of the literature and a description of the chemistry of chaulmoogra oil.

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¹ U. S. Pub. Health Rept., 1913, 28, p. 1855; 1914, 29, p. 21; Am. Jour. Trop. Dis. and Prevent. Med., 1914, 2, p. 300.

² New Orleans Med. and Surg. Jour., 1916, 69, p. 223.

³ U. S. Pub. Health Bull., 1916, p. 3.

⁴ Ann. Trop. Med. and Parasit., 1917, 11, p. 205.

⁵ Trop. Dis. Bull., 1919, 13, p. 13.

⁶ China Med. Jour., 1918, 32, p. 226.

⁷ Jour. Cutan. Dis., 1919, 37, p. 367.

⁸ Jour. Infect. Dis., 1920, 26, p. 238.

In 1915, Hernandez ⁹ reported that the addition of 2% chaulmoogra oil to culture mediums inhibited the growth of tubercle bacilli and had a favorable influence on tuberculosis in a few patients. Rogers ¹⁰ has also suggested the use of sodium chaulmoograte in the treatment of tuberculosis, but, believing that intravenous injections may produce exacerbations, has used instead the sodium salts of the fatty acids of cod-liver oil, believing that the favorable influence of the salts of fatty acids on acid-fast bacteria is nonspecific.

EXPERIMENTS

Our experiments were made with oil expressed cold from seeds of *Taraktogenous kurzii* King* and a strain (H) of bovine tubercle bacilli virulent for guinea-pigs. Since the oil was immiscible with mediums, a special technic was required for determining its possible germicidal activity for the tubercle bacillus. For this purpose the technic worked out by McMaster ¹¹ was adopted, the only modification being the substitution of agar slants by Petroff's solid medium and the use of 24-day cultures. Dilutions of chaulmoogra oil were made with sterile paraffin oil, the latter being entirely inert.

In the experiments the tubes of Petroff medium were well drained of water of condensation and inoculated with *B. tuberculosis* over an area of 1 cm. and well above the middle of the tube. These were incubated for 24 days. The oils were then poured over these so as to entirely cover the slant and the tubes were allowed to stand 24 hours in the incubator at 37.5 C. The oils were then poured off and the tubes twice washed out carefully with sterile salt solution. The growths were then transplanted to fresh slants of Petroff medium and incubated for 3 weeks.

With this technic our experiments were entirely negative; even pure undiluted chaulmoogra oil failed to kill all of the tubercle bacilli, as shown in table 1, giving the results of one of these experiments.

These results are in striking contrast to those of Walker and Sweeney,⁸ but our work was conducted with the whole oil while they employed the soluble sodium salts of the total fatty acids. Furthermore, McMaster's technic cannot be regarded as satisfactory for tests of this kind employing the tubercle bacillus because we were obliged

* Prof. Alsberg, Department of Agriculture, Washington, D. C., kindly supplied us with this oil.

⁹ Abstr. in Jour. Am. Med. Assn., 1918, 71, p. 1177.

¹⁰ Brit. Med. Jour., 1919, 1, p. 147.

¹¹ Jour. Infect. Dis., 1919, 24, p. 378.

to use cultures several weeks old which were frequently quite abundant. Even though some of the bacilli, and especially those in immediate contact with the oil, were destroyed, the deeper bacilli may escape and thereby mask any evidence of partial germicidal activity.

The next experiments were made with what may be called a combined in vivo-vitro technic, aiming to bring the oil into more intimate contact with the bacilli and testing for germicidal activity by injecting the mixtures into guinea-pigs.

TABLE 1
THE INFLUENCE OF CHAULMOOGRA OIL ON THE TUBERCLE BACILLUS EMPLOYING THE
McMASTER TEST TUBE METHOD

Dilution of Oil	Results	Dilution of Oil	Results
Undiluted	+	1:3000	—
1:5	+	1:4000	+
1:10	+	1:8000	+
1:100	+	1:10000	+
1:100	+	1:10000	+
1:500	—	1:16000	+
1:1000	+	1:24000	+
1:1000	+	1:32000	+
1:1500	+	Paraffin oil (control)	+
1:2000	+	Paraffin oil (control)	+

+ = subcultures showed growth of tubercle bacilli; — = subcultures sterile.

An emulsion of the bacilli was prepared by grinding cultures with sterile paraffin oil and placing 0.1 cc of the emulsion in flasks with 10 cc of varying dilutions of chaulmoogra oil (diluted with sterile paraffin oil). These mixtures were shaken mechanically with glass beads at room temperature for 18 hours and injected intramuscularly into guinea-pigs in amounts of 0.1 cc per 100 gm. of body weight. Controls employing pure paraffin oil alone were included in each experiment. The results were negative; even when the pure undiluted oil was employed, a sufficient number of bacilli escaped destruction to produce tuberculosis in guinea-pigs, as shown in the results of an experiment summarized in table 2.

This technic was rather favorable to any germicidal activity of the oil as it was brought into close contact with the bacilli for 18 hours at room temperature. The number of bacilli was not large and the dose injected into the pigs required 5 to 6 weeks to produce well marked inguinal adenitis and infection of the spleen and abdominal glands. However, even if but few bacilli escaped destruction, the results of inoculation into the young pigs would probably produce tuberculosis; therefore these experiments have shown the absence of

complete germicidal activity but have yielded no information on the question of partial destruction of the bacilli.

The next experiments were made by infecting young pigs with tubercle bacilli and administering the oil by intramuscular injection.

TABLE 2
THE INFLUENCE OF CHAULMOOGRA OIL ON THE TUBERCLE BACILLUS (IN VITRO-VIVO TECHNIC)

Dilution of Oil Acting on Bacilli	Duration of Lives of Pigs	Neeropsies
Undiluted.....	46 days	Generalized tuberculosis
1:5.....	16 days	Tuberculous adenitis
1:5.....	46 days	Generalized tuberculosis
1:10.....	37 days	Generalized tuberculosis
1:10.....	44 days	Generalized tuberculosis
1:100.....	49 days	Generalized tuberculosis
1:100.....	55 days	Generalized tuberculosis
1:1000.....	16 days	Tuberculous adenitis
1:1000.....	16 days	Tuberculous adenitis
1:10,000.....	55 days	Generalized tuberculosis
1:10,000.....	34 days	Generalized tuberculosis
1:100,000.....	20 days	Generalized tuberculosis
1:1,000,000.....	16 days	Tuberculous adenitis
No oil; culture control.....	46 days	Generalized tuberculosis
No bacilli; oil control.....	Lived in- definitely	No changes

TABLE 3
THE INFLUENCE OF CHAULMOOGRA OIL ON GUINEA-PIGS INFECTED WITH TUBERCULOSIS

Administration of Oil	Duration of Life	Neeropsies
First dose before infection; three doses later...	26 days	Tuberculous adenitis
First dose before infection; four doses later....	32 days	Tuberculous adenitis
First dose at time of infection; two doses later	26 days	Tuberculous adenitis
First dose at time of infection; nine doses later	57 days	Tuberculous adenitis
First dose one day after infection; three doses later	29 days	Generalized tuberculosis
First dose one week after infection; seven doses later	70 days	Generalized tuberculosis
Not infected; eleven doses of oil (control).....	Alive	Chronic myositis
Not infected; nine doses of oil (control).....	Alive	Chronic myositis
Infected (control); no oil.....	76 days	Generalized tuberculosis
Infected (control); no oil.....	22 days	Generalized tuberculosis

The inguinal glands of tuberculous pigs (5 weeks' infection) were emulsified with sufficient sterile salt solution to show only a few bacilli in stained smears of a loopful. These emulsions were then paper filtered and 0.2 cc injected subcutaneously into the abdomen. The untreated controls infected in this manner lived from 22 to 76 days before succumbing with general miliary tuberculosis.

The chaulmoogra oil was administered by intramuscular injection at weekly intervals in doses of 0.2 cc per 100 gm. of body weight.

Some pigs received the oil prior to infection, others received the first dose simultaneously with infection and others at varying intervals after infection, as shown in results of an experiment summarized in table 3.

The results have been of a negative character; when the oil was administered before or simultaneously with infection, the degree or extent of infection appeared to be confined to the neighboring glands in contrast to the generalized miliary tuberculosis which usually developed when the infection was given a longer start before the administration of oil was begun. As a general rule, multiple injections of the oil produced localized inflammatory changes at the sites of injection.

SUMMARY

Undiluted chaulmoogra oil (*Taraktogenos kurzii* King) and dilutions in paraffin oil, had no appreciable germicidal influence in vitro on a strain of bovine tubercle bacilli, according to the results observed with the technic employed in these experiments. The sodium salts of the total acids of this oil (chaulmoogrates) were not included in this study.

Undiluted and diluted chaulmoogra oil had no appreciable germicidal effect on virulent tubercle bacilli as determined by an in vitro-vivo method employing guinea-pigs.

Chaulmoogra oil in doses of 0.2 c c per 100 gm. of body weight administered by intramuscular injection at weekly intervals (equivalent to .2 c c per kilo or 120 c c per 60 kilos) had none or but slight effect on the course of tuberculosis in infected guinea-pigs.

Chaulmoogra oil is relatively nontoxic for guinea-pigs; animals have borne at least 11 intramuscular injections of 0.2 c c per 100 gm. without deleterious effect except localized inflammatory changes at the sites of injection.